REMARKS

Status of the Claims

Original claims 1-14 are pending. No claims are amended herein.

Rejection of Claims Under 35 USC 103

Claims 1-6, 8-10 and 12-14 were rejected under 35 U.S.C. §103(a) as obvious over Behr (WO 96/29087) in view of Jones (Nucl. Med. & Biol. 1996, 23:105-113) and Geerlings (US 5,641,471).

Claims 7 and 11 were rejected under 35 U.S.C. §103(a) as obvious over Behr (WO 96/29087) in view of Jones (Nucl. Med. & Biol. 1996, 23:105-113) and further in view of Griffiths (WO 96/40245).

Claims 1-6, 8-10 and 12-14 were rejected under 35 U.S.C. §103(a) as obvious over Buchsbaum (US 4,831,122) or Behr (WO 96/29087) in view of Jones (Nucl. Med. & Biol. 1996, 23:105-113) and further in view of Griffiths (WO 96/40245).

Applicants respectfully traverse the rejections. A prima facie case of obviousness requires: (1) a teaching or suggestion of all of the claim limitations; (2) a suggestion or motivation to modify or combine the teachings of the applied prior art; and (3) a reasonable expectation of success in reaching the claimed invention. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants note that the parent (USSN 09/588,565), of which the instant application is a divisional, issued as U.S. Patent No. 6,667,024. In the statement of Reasons for Allowance mailed on July 28, 2003, in the '565 application, Primary Examiner Michael G. Hartley acknowledged that, "there is no teaching in the prior art that provides the requisite motivation to combine at least two of the types of clearing agents recited in the claims." Applicants note that the scope of the issued claims in the '024 patent are almost identical to the instant claims, with the exception that the issued claims in the '024 patent are drawn to kits comprising at least two clearing agents, while the instant

claims are drawn to methods comprising use of at least two clearing agents. The combination of clearing agents recited is the same in the instant claims as in the issued '024 patent.

As discussed in detail below, Applicants submit that as of the instant priority date, there was no suggestion or motivation to modify or combine the teachings of the applied prior art to make the claimed combination (comprising at least two clearing agents) and the cited prior art actually taught away from making the claimed combination. Applicants further submit that the skilled artisan would have had no reasonable expectation of success in achieving the claimed invention as of the instant priority date.

The Office Action mailed 10/13/06 points to no suggestion or motivation in the cited prior art to modify or combine the teachings of the applied prior art. Rather, the Action asserts, without any support from the cited prior art, that, "One of ordinary skill in the art would have been motivated to include the chelating agent [of Jones] as an additional clearing agent in the cytotoxic reagent disclosed by Behr because the chelating agent taught by Jones, while having a similar effect as a clearing agent, provide an additional and separate advantage as compared to the clearing agent disclosed by Behr. For example, Behr teaches that the clearing agent reduces renal uptake of the radiolabled monoclonal antibody fragments (i.e., to both reduce toxicity and increase specificity), while the clearing agent taught by Jones provides the additional advantage of removing free radiometal, thereby reducing or preventing toxicity."

While Behr states that, "D-lysine is highly effective in reducing kidney retention of radioactivity in subjects that are treated with radiolabeled antibody fragments," Behr does not provide any suggestion or motivation to use other types of clearing agents in combination with D-lysine therapy. Behr is completely silent on the prospect of using different clearing agents other than lysine and would, therefore, not motivate one of skill in the art to use any clearing agents other than lysine. Therefore, Behr in reality motivates one to select only one type of clearing agent, i.e. a lysine-type clearing agent.

Because Behr provides no guidance or data on other types of clearing agents, one of skill in the art would have had no reasonable expectation of success in using any other clearing agents in combination with lysine. Based on the teaching of Behr, even in combination with Jones, one of skill in the art would not have known whether the use of additional clearing agents besides lysine would have reduced effectiveness, increased toxicity or produced undesirable side effects.

There is simply no showing in Behr of any combination of different types of clearing agents that would have provided the skilled artisan with any reasonable expectation of success in achieving the instant claimed methods.

Jones does not remedy the defects of Behr. Jones merely discloses that dithiol chelating agents are useful as potential adjuvants for anti-IL-2 receptor lead or bismuth alpha radioimmunotherapy. Like Behr, Jones does not provide any suggestion or motivation to use any other types of clearing agents in combination with dithiol chelating agents. Jones is completely silent on the prospect of using different types of clearing agents in combination with dithiols. Therefore, there is no proper basis for combining the teachings of Jones with Behr.

Since, like Behr, Jones provides no guidance or data on other types of clearing agents, one of skill in the art would have had no reasonable expectation of success in using any other clearing agents in combination with dithiols.

Geerlings is cited by the Action merely for the proposition that use of radioimmunoconjugates for therapy of cancer was well known as of the instant priority date. Since Geerlings is not cited for any teaching relevant to use of clearing agents, let alone the claimed combination of different types of clearing agents, it also fails to motivate the skilled artisan to make the claimed combination and provides no reasonable expectation of success in achieving the claimed combination.

Griffiths has specific language that teaches away from the use of other types of clearing agents. For example, Griffiths at page 9, lines 23-33 states that, "Because the clearing agents of the present invention bind to the primary binding site of the primary targeting species, they can only bind circulating primary binding species, and cannot bind species already bound to the target site. The clearing agents of the present invention therefore offer distinct advantages over clearing agents currently used, and avoid the problems discussed above. That is, the present clearing agents do not block the second binding sites of the primary targeting species and do not remove primary targeting species from the target site." (emphasis added)

Thus, the skilled artisan reading Griffiths would have been motivated to use only clearing agents that bind to the primary binding site of the targeting species and not any other type of clearing agents in combination. Griffiths teaches away from the use of any clearing agents that do not bind to the primary binding site of the targeting species, by characterizing other types of clearing agents as disadvantageous.

The Action cites page 10 of Griffiths for the proposition that, "Griffiths specifically teaches the use of more than one clearing agent in multiple steps." [Action at page 4, paragraph No. 5] However, the cited page discloses only that, following administration of a primary targeting species, "the clearing agent is administered to remove non-localized primary targeting species," and then administration of a second targeting species is, "followed by the administration of an anti-idiotype-antibody clearing agent according to the present invention."

While Griffiths may disclose the use of two clearing agents, the cited passage makes clear that they are both of the same type. I.e., both clearing agents recited on page 10 of Griffiths are designed to bind to the primary binding sites of targeting species (i.e., antibodies), as taught by Griffiths at page 9, lines 23-33. This would be no different from, for example, the use of two species of dithiol chelating agents in the method of Jones. There is simply no disclosure in Griffiths of using different types of clearing agents, acting by different mechanisms, as in the instant claimed methods. Nor would the skilled artisan, reading Griffiths, have any reasonable expectation of success in achieving the instant claimed methods, utilizing two or more different types of clearing agents.

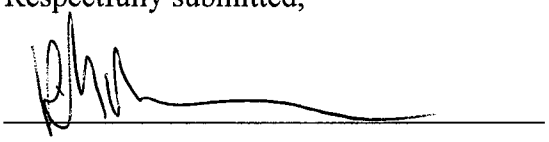
As with Geerlings, the Action fails to cite Buchsbaum for any disclosure relating to use of clearing agents, merely asserting that Buchsbaum, "discloses a radioimmunoconjugate comprising a cytotoxic beta emitting radionuclide bound to an tumor antigen-binding fragment of an antibody." Since Buchsbaum is not cited for any teaching relevant to use of clearing agents, let alone the claimed combination of different types of clearing agents, it also fails to motivate the skilled artisan to make the claimed combination and provides no reasonable expectation of success in achieving the claimed combination.

In summary, none of the cited prior art, alone or in combination, provides any teaching or suggestion in the cited prior art to modify or combine the teachings of the applied prior art. The skilled artisan, reading the cited prior art, would have had no reasonable expectation of success in achieving the instant claimed methods. Therefore, at least two of the three required elements to establish a prima facie case of obviousness are missing and rejection under 35 U.S.C. §103 is improper. Reconsideration and withdrawal of the rejection is respectfully requested.

Conclusion

For the reasons stated above, Applicants submit that the claims as amended are in condition for allowance and requests withdrawal of the rejections.

Respectfully submitted,



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